

## REMARKS

### Informalities

The disclosure was objected to as containing a hyperlink. By the foregoing amendment, the hyperlink has been deleted.

### The Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected Claims 1-11 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The second paragraph of Section 112 requires that the claims set out and circumscribe a particular area which applicants regard as their invention with a *reasonable* degree of precision and particularity.

a) The rejection indicates that in claim 1 it is unclear how “a protein mass tag (PMT) reagent” can be “differentially” labeled with “multiple chemical substituents.” Claim 1 has been cancelled.

b) The rejection indicates that in claim 1 it is unclear how the “protein mass tag” can be “differentially” labeled with only one “chemical substituent.” Claim 1 has been cancelled.

c) The rejection indicates that the exact composition of the “protein mass tag (PMT) reagent” of claim 1 cannot be determined and the two requirements are inadequate to chemically and functionally define the composition. Additionally, the rejection states that “certain protein functional groups” is unclear. Also, in claim 2, the rejection states that “homologous organic substituents” is unclear. Claims 1 and 2 have been cancelled. In claim 8 and 10, “certain protein functional groups” has been amended to recite “a protein component.” In claim 9, “homologous organic substituents” has been amended to read “organic substituents.”

d) The rejection states that in claims 4 and 5, the term “said protein functional group is an amino acid side chain” is inconsistent with conventional nomenclature wherein a “functional group” may be present on an amino acid side chain but is not, itself, “an amino acid side chain.” While Applicant believes the recitation of a functional group of an amino acid side chain is sufficiently definite, Claims 4 and 5 have been amended to that recite that the “protein component is an amino acid side chain,” in the interest of expediting prosecution.

e) The rejection states that the Markush group definitions recited in claim 6 are not conventionally acceptable definitions of the term “protein functional groups.” While Applicant believes the recitation “protein functional group” to be sufficiently definite, this term has been amended to recite “protein component” in Claims 4, 5, 6, 8, and 10, in the interest of expediting prosecution.

f) The rejection states that in claim 6, it is unclear what is meant by the terms “modified,” “a set,” and “digested.” In the interest of expediting prosecution, the recitation “a set of amino acids” has been deleted. In the interest of expediting prosecution, the recitation “modified” has been amended to recite “derivatized.” Support for this amendment can be found, e.g., at page 15, lines 7-16, which describes the derivatization of lysine. As explained in the specification, digesting proteins can be accomplished by a wide variety of methods familiar to those skilled in the art, and include cyanogen bromide (CNBr) digestion, or enzymatic digestion, e.g., with trypsin. (Specification, page 12, line 29, to page 13, line 2). Applicant therefore submits the term “digested” is definite.

g) The rejection states that is unclear what the difference in meaning is between the terms “differentially” in claim 1 and “differently” in claim 8. Claim 1 has been cancelled.

h) The rejection states that there is no antecedent basis for the term “protein reactive moieties” in claims 10 and 11. Claims 10 and 11 have been amended to recite “amino acid reactive moieties.”

i) The rejection states that it is unclear in claim 11 how the “protein reactive moiety reacts with *the side chain of an arginine*” since the only reactive portion of the side chain is a guanidinium group. Claim 11 has been amended to recite that the “amino acid reactive moiety reacts with arginine.”

It is believed that the foregoing amendments are sufficient to overcome the rejections under 35 U.S.C. § 112, second paragraph. Reconsideration is respectfully requested.

#### The Rejection under 35 U.S.C. § 102(b)

The Examiner has rejected Claims 1-11 under 35 U.S.C. § 102(e) as being anticipated by Aebersold, et al., U.S. Patent No. 6,670,194. The Examiner has also rejected Claims 1-4, 6 and 7 under 35 U.S.C. § 102(b) as being anticipated by Morgan, et al., U.S. Patent No. 5,840,712. The Court of Appeals for the Federal Circuit has stated that anticipation requires the presence in a

single prior art reference of each and every element of the claimed invention. *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed. Cir. 1984); *Alco Standard Corp. v. Tennessee Valley Auth.*, 1 U.S.P.Q.2d 1337, 1341 (Fed. Cir. 1986). "There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic v. Genentech Inc.*, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991) (citations omitted).

Solely in the interest of expediting prosecution, Claims 1-3 and 7 have been cancelled. Claims 4-6 have been amended to depend from Claim 8. Applicant reserves the right to pursue the cancelled subject matter in a continuing application.

The cancellation of claims 1-3 and 7, and the amendment of claims 4 and 6 renders the rejection of these claims over Morgan, et al., moot.

After the amendments, a single independent claim, claim 8, remains. Claim 8 claims a plurality of PMT reagents for mass spectrometric analysis of proteins each comprised of an amino acid reactive moiety that selectively reacts with a protein component, wherein each of said PMT reagents is differently labeled with one or more non-isotopic chemical substituents.

The rejection states that Aebersold, et al., describe affinity labeled protein reactive reagents having an affinity label covalently linked to a protein reactive group (PRG) through a linker. The  $-CH_2-$  groups of the linker can be substituted with different hydrocarbyl, alkoxy or functional groups. The compounds are not required to contain isotopes. The rejection further states that the "non-isotopic chemical substituents" are readable on the differentially substituted  $CH_2$  moieties of the Aebersold, et al., linker. The rejection further states that Aebersold, et al., at col. 5, lines 39-42, describes the "plurality of PMT reagents" of claim 8. The cited passage refers to "one or more affinity labeled reagents with different PRG groups . . . ." A PRG group, according to the immediately preceding sentence in the reference is "a group which selectively reacts with certain groups that are typically found in peptides." Therefore, Aebersold, et al., at this passage merely describes affinity labeled reagents with different groups that selectively react with groups found in peptides. That is, the reactive moiety, not the labeling moiety, is different in the different reagents.

Aebersold, et al., may suggest a plurality of reagents, but does not describe a plurality of reagents, wherein each of said reagents is differently labeled with one or more non-isotopic chemical substituents. The mere suggestion in Aebersold, et al., that the linker portion of the

Aebersold, et al., reagent can be substituted does not teach or imply that the substitution results in a plurality of reagents that are differently labeled with one or more non-isotopic chemical substituents, as required by claim 8. In fact, the only differential labeling that is described in Aebersold, et al., is *isotopic* differential labeling. There is no mention of *non-isotopic* differential labeling. The disclosure of Aebersold, et al., therefore, does not, contrary to the assertions of the rejection, contain all the elements of claim 8, as is required for anticipation. In sum, while Aebersold, et al., may suggest certain elements of Claim 8, the reference does not teach each element as claimed in Claim 8. Aebersold, et al., therefore can not anticipate Claim 8, or any claim depending from Claim 8.

Reconsideration is respectfully requested.

#### Closing Remarks

Applicant believes that the pending claims are in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Respectfully submitted,

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